

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 05 FEB 2007

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|---|---|---|-----------------------|
| Applicant's or agent's file reference<br>54-000330PC  | <b>FOR FURTHER ACTION</b>   |   | See Form PCT/IPEA/416 |
| International application No.<br>PCT/US04/22187   | International filing date (day/month/year)<br>07 July 2004 (07.07.2004) | Priority date (day/month/year)<br>07 July 2003 (07.07.2003) |                       |
| International Patent Classification (IPC) or national classification and IPC<br>IPC: C12P 21/02( 2006.01);C12N 1/21( 2006.01),15/74( 2006.01);C07H 21/02( 2006.01)<br>USPC: 435/69.1,488,252.33;530/399 |   |   |                       |
| Applicant<br>THESCRIPPS RESEARCH INSTITUTE  |   |   |                       |

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

a. ☐ (sent to the applicant and to the International Bureau) a total of \_\_\_ sheets, as follows:

☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

b. ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) \_\_\_\_\_, containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒ Box No. I Basis of the r

☐ Box No. II Priority

☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

☒ Box No. IV Lack of unity of invention

☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

☐ Box No. VI Certain documents cited

☐ Box No. VII Certain defects in the international application

☐ Box No. VIII Certain observations on the international application

Date of submission of the demand

22 December 2004 (22.12.2004)

Date of completion of this report

08 January 2007 (08.01.2007)

Name and mailing address of the IPEA/ US

Mail Stop PCT, Attn: IPEA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Facsimile No. (571) 273-3201

Authorized officer

Kathleen Kerr Bragdon

Telephone No. 571-272-1600

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/US04/22187

## Box No. I Basis of the report

## 1. With regard to the language, this report is based on:

- ☒ the international application in the language in which it was filed.
- ☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4(a))
  - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the elements of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

- ☒ the international application as originally filed/furnished
- ☒ the description:
- pages 1-80 as originally filed/furnished
- pages\* NONE received by this Authority on \_\_\_\_\_
- pages\* NONE received by this Authority on \_\_\_\_\_
- ☒ the claims:
- pages 91-97 as originally filed/furnished
- pages\* NONE as amended (together with any statement) under Article 19
- pages\* NONE received by this Authority on \_\_\_\_\_
- pages\* NONE received by this Authority on \_\_\_\_\_
- ☐ the drawings:
- pages \_\_\_\_\_ as originally filed/furnished
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☒ the sequence listing (*specify*): 81-90
- ☐ any table(s) related to the sequence listing (*specify*): \_\_\_\_\_

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to the sequence listing (*specify*): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/US04/22187

**Box No. IV Lack of unity of invention**

1. ☐ In response to the invitation to restrict or pay additional fees the applicant has, within the applicable time limit:
- ☐ restricted the claims.
  - ☐ paid additional fees.
  - ☐ paid additional fees under protest, and, where applicable, the protest fee
  - ☐ paid additional fees under protest but the applicable protest fee was not paid
  - ☐ neither restricted the claims nor paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:
- ☒ complied with.
  - ☐ not complied with for the following reasons:

4. Consequently, this report has been established in respect of the following parts of the international application:

- ☒ all parts
- ☐ the parts relating to claims Nos. \_\_\_\_\_

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.  
PCT/US04/22187**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

|                               |   |     |
|-------------------------------|---|-----|
| Novelty (N)                   | Claims <u>1-55 and 59-65</u>                      | YES |
|                               | Claims <u>56-58</u>                               | NO  |
| Inventive Step (IS)           | Claims <u>5-8, 10-15, 17, 20, 22-55 and 59-65</u> | YES |
|                               | Claims <u>1-4, 9, 16, 18, 19 21 and 56-58</u>     | NO  |
| Industrial Applicability (IA) | Claims <u>1-65</u>                                | YES |
|                               | Claims <u>NONE</u>                                | NO  |

**2. Citations and Explanations (Rule 70.7)**

Claims 1-55 and 59-65 meet the criteria set out in PCT Article 33(2), because the prior art does not teach or fairly suggest the specific Orthogonal RS and orthogonal tRNA molecules and the use of these specific orthogonal pairs for the production of proteins having the unnatural amino acid homoglutamine (see reasoning below).

Claims 56-58 lack novelty under PCT Article 33(2) as being anticipated by Bednar et al. Bednar et al teach modification of cysteine residues in an enzymatic protein (chalcone isomerase) to introduce a neutral homoglutamine analogue ( see abstract).

Claims 5-8, 10-15, 17, 20, 22-55 and 59-65 meet the criteria set out in PCT Article 33(3) because the prior art does not teach the specific Orthogonal RS and orthogonal tRNA molecules and the use of these specific orthogonal pairs for the production of proteins having the unnatural amino acid homoglutamine.

Claims 1-4, 9, 16, 18, 19 and 21 lack novelty under PCT Article 33(3) as being obvious over Schultz et al (WO/02/085923 A2) in view of Terada et al. Schultz et al teach methods of producing orthogonal tRNA synthetases from wild-type tyrosine-tRNA synthetase or orthogonal tRNA synthetases from leucine and the corresponding orthogonal tRNA for tyrosine or leucine respectively. Schultz et al teach the use of such O-tRS/O-tRNA pairs in in-vivo incorporation of one or more unnatural amino acids into proteins of interest. Schultz et al also teach generation of selector codons having four or more base codons (see page 34-35). In addition Schultz et al teach that a large number of sources and host organisms from which the O-RS can be derived including from *Pyrococcus horikoshii* (see page 32). It would have therefore been obvious for a person skilled in the art to use the method of Schultz et al to produce O-RS that can be used with a corresponding O-tRNA derived from any source. One of skill in the art would use tRS for which the structures have been studied and have been found to have overlapping structural similarities to other amino acids such as the case with *Pyrococcus horikoshii* lysyl RS which show a high degree of structural similarity to *Thermus thermophilus* glutamyl tRNA synthetase as taught by Terada et al.

Claims 1-65 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

## ----- NEW CITATIONS -----

Bendar et al. Introduction of unnatural amino acids into chalcone isomerase. *Bioconjug Chem.* July-August 1991, Vol. 2 No. 4, pages 211-216. Abstract.